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## EDITORIALS

### "TWENTY THOUSAND DOCTORS CAN'T BE WRONG!"

**T**WO INTRIGUING questionnaires came in the chaff-laden mail of a doctor friend of mine the other morning. One solicited his reactions to certain tobacco queries, the other naïvely inquired about coffee. Each came *allegedly* from an organization searching for truth and motivated by the most altruistic ideals. Actually they were wily ambassadors of wilier advertising agencies—sent more than likely to every doctor in the land—in search not of facts but of opinions, seeking not for truth but for commercially useful and usable statements and misstatements.

In my doctor friend's office they were unceremoniously dumped, despite a crackling cellulosic protest, into that reticulated repository commonly known as the waste basket.

But not all the doctors who received these inquiries dealt as sanely with them as this doctor did. In proof of which note that one of these days our leading and misleading magazines will break out in an advertising rash something like this—

**"Twenty thousand doctors find no fault in Old Camsterfield  
Cigarettes. Not a choke in a cartload."**

and

**"American Medicine Recommends Nokaffee Koffee."**

"You may dunk, you may drown, in this drink, if you will,  
But the kick of the caffeine is perfectly still."

For this testimony "American medicine" may or may not have received one carton of said cigarettes and one pound of the aforementioned and alleged coffee—which seems like excessive payment.

But such a tricky technic as this is not worthy of any advertising agency and is on a par with those gall-tinctured quackery promoters who conclude their copy with the hackneyed and downright disreputable statement—

**"Recommended by All Reliable Druggists."**

That phrase is a calumny and an unwarranted insult to pharmacy.

Reliable druggists *could not* and *do not* recommend such flim-flammers and frauds.

IVOR GRIFFITH.

### "THE CHEMICAL FORMULARY"

**A** FEW months ago the writer was requested to collaborate with a selected group of industrial chemists in the compilation of a new Chemical Formulary. He refused on the ground that the project seemed neither usual nor ethical.

The *mimeographed* communication of request came on the letterhead of the Glyco Products Co., Brooklyn, New York, a concern selling and manufacturing a large variety of natural and synthetic plastics, resins and waxes.

The aforementioned formulary is now a reality. Clad in its brilliant scarlet cover and comprising nearly six hundred pages it offers a "condensed collection of valuable, timely, practical formulæ for making thousands of products in all fields of industry."

In common with most formularies of its kind it can be truly said that even if India paper had been used in its construction there would still be too much distance between its covers. Equally true is it that it does contain much that is practical and useful.

But its context certainly justifies the good judgment of those persons who refused to collaborate in its compilation.

It is neither usual nor ethical.

To digress a little, but by way of illustration—certain proprietors of patent medicines a few years ago hit upon a most successful and ingenious method of promoting the sale of their quackeries. They would christen their product with a coined name, somewhat suggestive of a medicament. Around this named product its capital initial letter humbly but purposely avoided the advertising genius would build a seemingly simple formula of known and valuable remedial agents. This legitimate looking formula was then published and recommended in its entirety for the treatment of common ailments.

The false proprietary was thus obscured and its sale promoted by as fine a piece of advertising psychology as ever found its way to practice.

Millions of dollars in profits were thus made on such frauds as kargon, mercolized wax, and other similar products.

But what has all of this to do with the Chemical Formulary?

Just this—that although the analogy is but partly correct—this Formulary masquerades as a scientific work of worth when its designed purpose is to promote the sale of specialties and proprietaries deftly hidden in the context of the diversified formulas in the book.

Mind you—the analogy used had to do with quackeries—whereas the formulary has not. But the method is just as unethical and unscientific and unsound as that of the clever writer of copy for quacks.

Take, for instance, this formula for lubricating jelly (page 383):

Karaya gum .....	7.5 gm.
Glycomel .....	10.0 gm.
Isohol .....	5.0 gm.
Water .....	100 cc.
Moldex .....	0.15 gm.

Glycomel, isohol and moldex are specialties made only by Glyco Products Co., Brooklyn, N. Y., who seem to be the guiding spirit in the whole project.

To compile an alleged scientific formulary on a premise such as this is as reprehensible and unethical as another practice employed by this same organization, namely the printing upon their advertising leaflets for plant chemists, the following intriguing notice—

*“Chemists Attention”*

“A royalty will be paid for bringing to our attention uses for our products which are actually adopted.”

No further comment is necessary.

IVOR GRIFFITH.

## BEFORE VITAMINS!

(Editorial Note.—This is a fragment of an old lecture delivered by Professor Lloyd in 1878. Note how well he anticipated the vitamins.)

**T**URN YOUR MINDS to your old lectures in the Eclectic Medical Institute. Consider remedies used in treating an ailment (or ailments) then titled 'scrofula.' These remedies were bunched as 'antiscorbutics,' a term given any vegetable substance that tended to alleviate so-called 'scrofula,' which, as has been stated, was in itself a term applied to a complexity of ailments connected with tuberculous degenerations, especially glandular.

"Not of the disease shall I speak. That is out of the sphere of the pharmacist or chemist, but of the *things* having antiscorbutic qualities, or supposed to have them, then used to treat the ailment. Among these, lemons and oranges may be named as prominent 'antiscorbutics.' But in my old lectures I did not rest thought with such as these. Any vegetable food that came in the springtime was included—yes, suggested—as dominating even these citrous fruits.

"Eat freely of the early vegetables, prescribe them to your "run-down" patients. Begin with the common "garden stuff," eat freely, especially of such as you crave. They carry little, if any, "scientific" qualities, but they are loaded with *supportives* (a term coined by me to apply to such substances). Do not neglect sassafras tea as a spring-time tonic.'

"Turn to any 'Chemistry of Foods' and note that precious little starch or sugar is found in lettuce. But when comes springtime we crave lettuce, which carries structures that correct ailments caused, perhaps, by the excess of starch, sugar and meat foods that have been consumed during the winter.

"Turn to the young onion, which I advise you to eat, top and bulb, chopped fine, on a side dish with vinegar, salt and pepper. The young onion carries incalculable '*supportives*' not found in the onion carried over the winter—'antiscorbutics,' as the soldiers in the army and members of Franklin's expedition to seek the North Pole discovered. To this it may be added that the *young onion* carries a colloidal, slippery serum or juice not present, or at least scarcely present, in the full-grown onion; and that the young onion top carries an abundance of the vitalized green known as *chlorophyl*, which word has long been known, but which substance is no more valued in works on medical



science than is sand accepted as other than a cumberer of the earth in which the onion grows.

"Listen. But if there were no earth substance there could be no 'onion chlorophyl,' or any other plant green, and I say to you now that if there were no plant green there could be no vegetation, and were there no vegetation there could be no animal life. On chlorophyl and its mysterious transformations all sunshine-bred plant life depends for existence.

"Think, then, this lecture over, but turn not to your books, which live on and delight in carbohydrates, such as sugar and starch. In books scarcely will you find chlorophyl and its brother associates, the green of vegetation (pure chlorophyl in bulk is black), counted worthy of any consideration.

"But remember, I tell you they are *life supportives* and life creators of the entire vegetable as well as animal kingdoms.

JOHN URI LLOYD."

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#### **American Pharmaceutical Association Officers-Elect for 1934-1935**

The Board of Canvassers of the American Pharmaceutical Association, has announced as the result of the mail ballot for officers of the association, the election of the following:

President, Robert P. Fischelis, Trenton, N. J.

First Vice-President, George D. Beal, Pittsburgh, Pa.

Second Vice-President, Oscar Rennebohm, Madison, Wis.

Members of the Council (for three years): H. A. B. Dunning, Baltimore, Md.; S. L. Hilton, Washington, D. C.; W. Bruce Philip, Washington, D. C.

These officers will be installed at the next annual meeting of the association which will be held in Washington, D. C., the time to be announced later.

## ORIGINAL ARTICLES

### A CONTRIBUTION TO THE PHOTOCHEMISTRY OF COD LIVER OIL\*

By J. Howard Graham

**S**TUDIES in connection with the properties of cod liver oil have filled volumes, and there seems to be no tendency to stop effort along this line. While for centuries cod liver oil was being used as a medicine, there was mystery attached to its beneficent qualities, and it was used only empirically. Now that it is known for a certainty that cod liver oil contains at least two vitamins "A" and "D", perhaps in quantities exceeding other natural sources, and that the valuable properties of the oil are due largely to the presence of these vitamins, research has been stimulated to a marked degree. Each contribution has emphasized the generally recognized fact, that cod liver oil is one of the most complex natural substances known. Consequently it has offered problems that have appeared almost unsolvable. Thanks however to the research endeavors of many of our industrial and pharmaceutical laboratories, due primarily to an effort to place before the public a more perfect and stable preparation, light is gradually being thrown upon the constitution and keeping qualities of this valuable product, and thus, coincident with the more perfect maintenance of the original qualities of the oil, which requires knowledge and care not attributed to the layman, certain legislation has been recently passed (1) regarding those who are to be permitted to sell this product.

#### PHYSICAL AND CHEMICAL PROPERTIES

This paper concludes fifteen months' research undertaken to satisfy a curiosity with regard to possible changes in certain properties of cod liver oil in connection with which there is a dearth of experimental evidence recorded. Before stressing this side, however, a very brief and by no means exhaustive review of the physico-chemical knowledge of cod liver oil will be submitted as taken from recent literature. It should be made clear, however, at this point, that every set of constants of cod liver oil published in treatises on fats, emphasizes its indefinite nature.

A pure Norwegian cod liver oil has a pale yellow color (Taub (2) discusses a permanent color standard for U. S. P. cod liver oil);

\*Read at the Fifty-sixth Annual Meeting of the Pennsylvania Pharmaceutical Association, June 29, 1933.

has a Sp. Gr. of 0.9291; Iodine number of 168.5; Saponification number of 191; unsaponifiable matter 1.60 per cent.; free fatty acids 0.42 per cent.-1.10 per cent. (3)

It contains among other things (4), saturated fatty acids; non-saturated monoethylenic acids; other non-saturated acids; unsaponifiable matter such as cholesterol; bromine; iodine; biliary matter; organic bases; vitamin "A". To this, research has added and confirmed vitamin "D". (29) Möller (5) in 1895, listed more than fifty compounds alleged to occur in rotted cod liver oil.

In medicinal cod liver oil, the nitrogen content is at most 1 mg./100 g., and the phosphoric acid calculated as P, is 0.1 mg./100 g.

#### ACTION OF LIGHT

Attention is to be directed primarily to the action of light on cod liver oil. This light action will naturally include effects contributed by moisture and varying quantities of oxygen as air. Peacock (6) has summarized very comprehensively the findings of many investigators, when he says, that the exposure of normal cod liver oil to any source of white light of sufficient intensity, results in the following changes:—

(1) The normal bright golden fluorescence of the oil progressively disappears, this effect being termed "delumination".

(2) Before full "delumination" occurs, the oil fails to give the arsenic chloride test for vitamin "A".

(3) Fully "deluminated" oil when kept for some months in the dark, slowly regains much of its fluorescence, but the vitamin "A" appears to be permanently destroyed.

(4) There is a change in the absorption spectrum corresponding with the change in fluorescence of the oil. As "delumination" proceeds, so the transmission spectrum extends into the ultra-violet region. As the fluorescence returns, there is a proportionate return of the absorption spectrum.

As a result of investigations, it is shown that light is a variable factor which must be taken into account in all quantitative experiments concerning the growth promoting properties of cod liver oil and the manner in which such oil is stored; and attention is directed to the unusual nature of the complex reaction of cod liver oil to light, a reaction which is only partially reversible.

Norris and Church (7) say that the chromogenic substance of cod liver oil, or vitamin "A" is rapidly destroyed by light of wave length less than  $500\mu$ , but is practically unaffected by longer wave lengths. The rate of destruction by light is accelerated by the presence of oxygen.

Price (13) shows that an oil exposed to sunlight for a short time has had its effect on calcium metabolism increased, but that prolonged exposure results in the formation of poisonous substances.

Lea (8) makes the following contribution, where he says, that light accelerates the oxidation of fats, and that the reaction is autocatalytic. Exposure to direct sunlight produces rancidity even though the period of exposure be only a few minutes. The content of active oxygen (organic peroxides), and the response to the Kreis reaction for rancidity (the formation of a pink color with phloroglucinol and hydrochloric acid in ether-benzene solution), tend to increase simultaneously. Low temperatures favor the formation of peroxides, and bright sunlight the development of rancidity. The acidity of the fat is not influenced, at least during the earlier stages of these changes.

Experimental data on the development of rancidity will be furnished later; but at this time it will be worthwhile to note the definition of rancidity as given by Kerr (9). He defines rancidity as a chemical change in a fat due to the action of oxygen. Its development and progress are accelerated by certain accessory factors, notably light, heat, presence of moisture and contact with certain metals, but oxygen is absolutely essential. Without oxygen there can be no rancidity. He further says that aldehydes, ketones and acids of less molecular weight than those originally present, seem to be the constant constituents of rancid fats.

With regards to the Kreis (10) reaction, Kerr (9) confirms certain objections raised by Winchel, but at the same time, suggests an improvement which has been employed in the following research and will be described later.

#### **ACTION OF OXYGEN**

That oxygen performs a very definite function is evidenced by the oxidation numbers obtained by Issoglio (11) where in using 100 g. of oil that had been distilled with steam, the yellowish oil gave numbers which ranged from 1.84-8.07, while the brown unpurified oil gave numbers ranging from 20.42-38.42.

Bills (5) remarks that it is quite evident that the oxidation of cod liver oil is an autocatalytic process accelerated by organic peroxides and retarded by foreign substrates.

Schimkus (12) found that an oil exposed to sunlight for several hours had a peroxide concentration of 0.01 Normal. This will act in a catalytic manner on anions of iodine to form elementary iodine.

Most of the crude cod liver oils respond to a modified Schönbein (15) procedure for the detection of peroxides. This test is given as follows:—two reagent solutions are prepared freshly as follows: 0.1 per cent. hemoglobin in water, and 0.5 per cent. guaic in absolute alcohol. Prepare 10 cc. of oil in one test tube, shake well with 10 cc. absolute alcohol and set aside for the separation of layers. In another test tube 5 cc. each of the guaic and hemoglobin solutions are mixed with 5 cc. of the alcoholic extract (above) and well shaken. In the presence of peroxides a blue color will develop in a few minutes, the rate of development being clearly proportional to the peroxidation of the oil.

Briod and others (14) say that high oxidizability values are supposed to indicate rancidity, but that this is not the case with cod liver oil because fresh samples often respond to the Kreis test for rancidity.

When a current of oxygen is passed through cod liver oil separated by glass from a photographic plate, the plate is not affected; but if the separation is made by quartz, the photographic plate is blackened.

In connection with oxygen absorption, it is reported (17) that clothes semi-saturated with cod liver oil in a currying shop for leather, took fire without warning.

An early experiment on the oxidizability of cod liver oil is described by Thomson and Dunlop.(18) They examined an oil which had been kept in a bottle for over three years with no attempt to exclude all air. It gave a Wijs number of 156.5; saponification number of 191.4; free acid 1.24 per cent.; Reichert-Wollny value of 2.0. In their opinion the Reichert-Wollny value for a fresh oil is less than one; but in the partially oxidized oil it may exceed three. This would point to an increase in volatile acids.

Holmes (19) says that "Blowing" with air causes an oil to have the vitamin content which it originally had, decreased, due to the oxidizing effect of the air.

Goldblatt and Soames (20) say that the quartz mercury light synthesizes the antirachitic factor, vitamin "D", and yet excessive illumination causes the cod liver oil to lose this activity.

Holmes (21) says further that the sulphuric and nitric acid color tests show that light, air and moisture cause some change in cod liver oils during a period of six months. That therefore the oil should be promptly bottled and sealed. He adds that upon analysis of 111 samples of known origin, all met U. S. P. specifications but that there was no regularity in analytical results.(23)



Lewkowitsch (24) uses several pages of his treatise to a review of research with oils exposed to light alone, and then to light in the presence of air and moisture. Some experimenters, he says, have shown that when air is rigidly excluded, there is no change produced which would lead ultimately to rancidity. This finding is contradicted by others who had the experience with fats becoming distinctly rancid with an increase in free fatty acid after sealing for two years in glass tubes filled with nitrogen. It is stated that the greater the proportion of unsaturated fatty acids (as measured by their iodine absorption), the greater is their power to absorb oxygen.

The effect of moisture is a far-reaching one. Hydrolyzing enzymes seem to occur in most vegetable oils and to a lesser degree in animal oils. Accepting as a fact that they do occur in animal oils, we are able to understand better the changes which occur in oils when exposed to atmosphere and light. In the presence of sufficient moisture and acid, enzymes will bring about the production of diglycerides, monoglycerides, and free fatty acids within a comparatively short time. Lewkowitsch ascribes as the primary cause of rancidity the formation of free fatty acids as a result of the presence of moisture and soluble ferments. It has been shown that the exposure of oleic acid to air and sunlight for a week developed nonylic acid,  $C_8H_{17}COOH$ , and azelaic acid,  $C_7H_{14}(COOH)_2$ , and corresponding aldehydes, the same products as produced by exposure to ozone. The Kreis reaction used as a test for rancidity, and upheld to a certain extent by Kerr, (9) Lewkowitsch finds to give very erratic results. He concludes by saying that it may be taken as proved that rancidity is due to the simultaneous action of water, oxygen and light, and that there is very little known as to the chemical change which the liberated free fatty acids undergo.

Cod liver oil is very prone therefore to important and harmful changes as to color, vitamins, and the nature of the glycerides and other substances present, when subjected to the influence of light, moisture and temperature changes. To protect against these changes patents (25) have been taken for packing in receptacles filled with inert gas such as carbon dioxide and nitrogen, particularly protecting against the oxidation of the vitamins.

#### EXPERIMENTAL

The investigation which is the background for this paper was undertaken to ascertain if possible,

I. Whether measurable quantities of probable nitrogenous substances are evolved during the saponification of the cod liver oil.



2. Whether there is correlation among the saponificatoin number, the iodine and free acid values for oils exposed over months of time.

3. And for a study of any development of rancidity as revealed by the Kreis and the Hager-Salkowski tests for the same.

Four specimens of oil were examined, A, B, C and D. With only the first three were attempts made to estimate any volatile nitrogenous bases, probably amines. With only the fourth specimen were the saponification number, iodine number and free acid percentage obtained.

#### **VOLATILE BASES**

Slightly over eight grams of oil on the average were saponified with 100 cc. of half-normal alcoholic potash, while twenty-eight liters of air were drawn through during a period of one hour and at the boiling temperature of water. Any volatile base was estimated by absorption in tenth-normal HCl. The results did not prove highly satisfactory with the amount of material used, and they will be stated only in a general way; but they present an opportunity for a separate and more elaborate investigation.

Several specimens of	Time of exposure days	Absorption of N/10 HCl cc.
A, B, C	Unexposed	variation from 0 to 0.1
A	0 to 12	increase from 0.1 to 0.35
B	0 to 12	increase from 0.1 to 0.45
C	0 to 25	increase from 0.1 to 0.15

These results seem to be of no further value than to indicate that during the first twenty-five days' exposure, traces of some volatile basic substance or substances are liberated.

#### **PREPARATION OF THE SPECIMENS**

Of the cod liver oils, A and B were well-known products purchased in pint bottles. They were transferred to oil sample bottles, corked and with varying quantities of air, exposed to light and weather. Specimens C and D were secured through the generous co-operation of one of our pharmaceutical laboratories.(26) They were taken from tin-lined metal drums and transferred to ampules; C with approximately 25 cc. of air and D with approximately 5 cc. of air. All ampules were sealed and exposed thus outdoors.

That all four specimens were different, at least as to their stearin content is indicated by their behavior upon chilling.

A was yellow and deposited no stearin at 32 deg. Fahr.

B was very yellow and deposited a slush of stearin at 32 deg. Fahr.

C was yellow, was cloudly at 32 deg. Fahr., but semi-solid at 14 deg. Fahr.

D was yellow and deposited no stearin even at 14 deg. Fahr.

Cod liver oils differ very much with respect to the deposition of stearin. Éwe (27) has examined twenty-two specimens of cod liver oil. All remained clear at 20 deg. Fahr., nine were clear at 18 deg. Fahr., and two were clear at 10 deg. Fahr.

The Kreis reaction as modified by Kerr, (9) and the Hager-Salkowski (28) reaction as described by Bills (5) were applied to all specimens in a routine manner. The results are summarized below without giving the intermediate gradations of color or shade.

Kreis test:—10 cc. of oil were placed in an 8 x 1 in. tt.; 10 cc. con. HCl were added, a rubber stopper inserted, and the tube thoroughly shaken. There is then added 10 cc. of 0.1 per cent. solution of phloroglucin in ether, the tube is closed and shaken as before. The appearance of a pink or red color in the acid layer indicates some degree of rancidity.

Hager-Salkowski test:—to a drop of oil dissolved in 1 cc. of chloroform or carbon disulphide there is added one drop of con.  $H_2SO_4$ . The development of a violet or purple color passing slowly to brown, indicates a possible freedom from rancidity.

Specimens corked in oil sample bottles				Reaction to Hager-Salkowski test
Oils	Exposure days	Color resulting	Dark closet days	
A	0	yellow		white to brown to yellow-brown purple passing to brown
A	90	faint yellow		
A			0	
A			90	
A	210	colorless		
A		deep yellow	210	
B	0	yellow		
B	90	faint yellow		
B			0	
B			90	

Specimens sealed in ampules					
Oils	Exposure days	Color resulting	Dark closet days	Reaction to Kreis test	Reaction to Hager-Salkowski test
C	0	yellow		faint pink	purple, passing to brown
C	47	less yellow		faint pink	no purple, red-brown
C	158	faint yellow		purplish pink	" " , brown
C		yellow	0	faint pink	purple, passing to brown
C		deep yellow	158	brown red	" " "
D	0	yellow		faint pink	purple, passing to brown
D	92	faint yellow		purplish pink	no purple, brown
D		yellow	0	faint pink	purple, passing to brown
D		yellow	100	faint pink	purple, fading slowly

### Summary

In the course of about ninety days it is observed that the golden yellow fluorescence, due according to Lewkowitsch (24) to the presence of lipochromes and to cholesterol, has disappeared, with a resulting pale yellow or almost water-white oil.

Similarly the pink color of the Kreis test, noticeable with all specimens of these oils, at the start, develops more rapidly, giving rise to a faint purple similar to weak  $\text{KMnO}_4$  solution, and with the specimens kept in dark closet, to a deep red color.

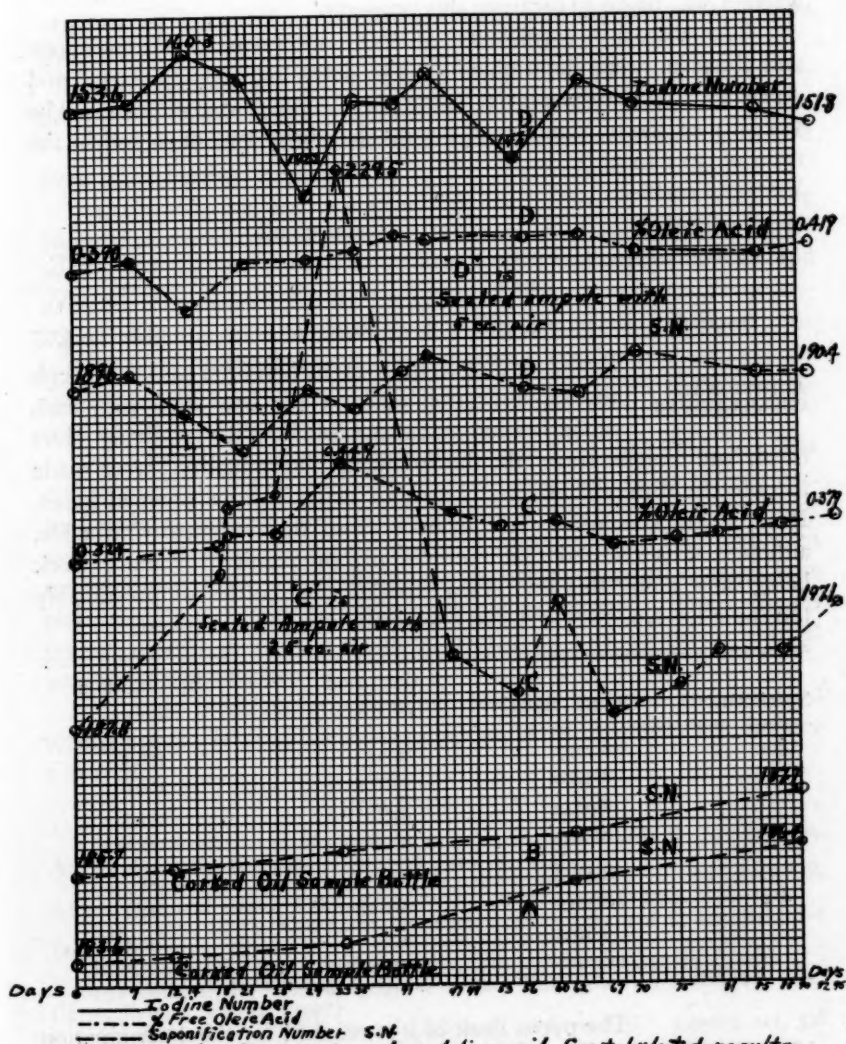
The purple, or reddish blue, of the Hager-Salkowski test, developing at first immediately and of about one second's duration, gradually gives way to an immediate formation of a brown color followed by a brown precipitate.

In the author's opinion, the Hager-Salkowski reaction is much more conclusive in determining effects of light exposure and rancidity than the apparently more delicate Kreis reaction.

The saponification number, the Hübl iodine number and the per cent. free acid, as oleic, were determined in several specimens, and under varying conditions of exposure, and time, by methods described in detail in Lewkowitsch. (24) The results are tabulated below. A ninety-five day portion of the results are represented by the accompanying graph.

**SAPONIFICATION  
AND IODINE  
NUMBERS; PER  
CENT. FREE ACID**

Specimen	Grams taken	Exposure days	Saponification value	Iodine value	% free acid as oleic
Corked in oil sample bottle					
A	8.4955	0	183.6	(not determined)	
	8.1365	12	183.7	"	"
	8.0445	33	184.0	"	"
	8.0651	62	185.5	"	"
	9.6260	90	186.4	"	"
	8.2736	210	190.9		0.550
		dark closet			
	8.3976	210	192.4		0.760
Corked in oil sample bottle					
B	8.2258	0	185.7	(not determined)	
	8.1493	12	185.9	"	"
	8.0615	33	186.3	"	"
	8.1902	62	186.7	"	"
	8.3485	90	187.7	"	"
Sealed in ampule with 25 cc. air					
C	8.2578	0	187.8	not determined	0.324
	9.0000	18	199.5	"	0.345
	8.1918	19	204.8	"	0.357
	8.0584	25	205.4	"	0.359
	8.0667	33	229.5	"	0.449
	8.2231	47	193.2	"	0.382
	8.1591	53	191.5	"	0.361
	8.0733	60	197.3	"	0.375
	8.0431	67	188.3	"	0.343
	8.5037	75	191.0	"	0.348
	8.7199	81	193.6	"	0.360
	8.1277	88	193.6	"	0.363
	8.2320	95	197.1	"	0.379
	this far, plotted as graph				
	8.4109	102	192.8	"	0.353
	8.1789	109	190.3	"	0.349
	8.0456	116	192.8	"	0.351
	8.0298	123	186.5	"	0.352
	8.7055	130	192.4	"	0.347
	8.0339	137	191.7	"	0.353
	8.1485	144	197.9	"	0.376
	8.0759	151	192.4	"	0.366
	Sealed & dark closet				
	8.3578	158	191.3	"	0.339
Sealed in ampule with 5 cc. air					
D	8.4330	0	189.6	153.6	0.390
	8.1936	7	190.3	154.1	0.398
	8.0264	14	187.7	160.3	0.338
	8.3993	21	184.8	157.5	0.387
	8.1302	29	189.4	142.2	0.400
	8.4920	35	187.9	154.5	0.408
	9.6830	41	190.6	154.2	0.429
	8.0625	49	191.8	157.7	0.422
	8.4231	56	189.5	147.1	0.422
	8.1681	63	189.2	157.0	0.429
	8.3460	70	192.1	154.2	0.412
	8.3473	85	190.5	153.3	0.405
	9.1676	92	190.4	151.8	0.419
	unexposed, dark closet				
	8.1267	100	194.7	159.2	0.423



A, B, C, D Samples of cod liver oil - See tabulated results



**VISCOSITY**

With the observation that the viscosity of the oil specimens changed upon long exposure to light, an attempt was made to measure this property.

The viscosity coefficients of "D" specimen of oil, trials one and thirteen, were determined on the dates January 25, 1933, and April 27, 1933, respectively, using the Ostwald viscosimeter. The viscosity of the oil diminished during the ninety-two days and in the ratio of 59.1 to 57.7.

Viscosity coefficient of water  
at 22 deg. C.

V

0.00806

Unexposed oil

U

0.47688

Exposed oil

92 days

E

0.46524

U

 $\frac{U}{V}$ 

59.1

E

 $\frac{E}{V}$ 

57.7

**ADDITIONAL  
OBSERVATIONS**

Realizing that 28 liters of air had been passed through the saponification mixture for one hour with each saponification made, and knowing the oxidizing effect of air and oxygen upon oils, the following determinations were made to note the different effects, if any, of using various purified gases. Results and conclusions are evident from the accompanying table, although it is realized that there is an opportunity for more work being done along this line. Two separate pint bottles of presumably the same lot No. 782517A (26) were contributed to this end.

Specimen	Grams taken	Gas used 28 liters	Saponification number
#1	8.2127	none	186.5
	8.3640	nitrogen	186.8
	8.0622	air	191.3
	8.5449	oxygen	187.8
#2	8.0402	none	188.7
	8.3925	nitrogen	188.2
	9.6103	air	194.4
	8.2345	oxygen	193.5

**LOSS IN WEIGHT  
OF PYREX FLASK**

The pyrex flask of 250 cc. used for the determination of fifty-eight saponification numbers, where the lower surface was acted upon for one hour each time by 100 cc. N/2 alcoholic potash, lost 1.4237 grams, or, an average of 0.0245 g. per determination.



### Conclusions

1. From the foregoing results, there appears to be no conclusive evidence of consistent correlation among the saponification, iodine and free acid values.

2. Variations of air, moisture, light and temperature conditions, seem to preclude any possibility of close correlation.

3. A realization of the complexity of the chemical nature of cod liver oil is further emphasized.

4. Considering the two generally used tests for rancidity, the Hager-Salkowski would seem to be more preferable to the Kreis in determining the relative freshness of an ordinarily handled cod liver oil. Even with the first mentioned test, the purplish blue obtained with the specimens of fresh oil, will continue to appear, for periods up to thirty-five days; but whereas the color lasts at first for approximately a second, the purple color becomes ever more evanescent as the days increase.

5. The reports of all investigators seem to point to the fact that cod liver oil should be prepared properly and handled as rapidly and as cleanly as possible, with the exclusion of excessive moisture, light and air, and with the maintenance of comparatively low and even temperatures, since it is realized that important chemical changes take place rapidly if proper conditions are not maintained. There should be and usually there is, a scientific control of this important natural and beneficent product.

6. This investigation does not close the book on cod liver oil examination. It manifestly opens up numerous avenues for further research.

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### The New Law and the Dispensing of Drugs in Japan

Japanese pharmacists have for a long time been making an effort to deprive physicians of the privilege of dispensing their own drugs but in vain. In the new medical laws, which become effective this fall, there is the following statement: "When a physician is requested to write a prescription instead of giving medicine to a patient, he shall write a prescription, so long as it is no hindrance to treatment." This is supposed to be the entering wedge to the division of the dispensing of drugs between pharmacists and physicians. The latter, of course, are not eager for a law of that kind, but public opinion, as shown by editorials in the daily papers, is for the amendment. Pharmacists have increased greatly in number since 1931. The increase in physicians has not been proportionate.—(J. A. M. A.)

## NOTES ON THE ASSAY OF STRYCHNINE ALKALOID IN STRYCHNINE SULPHATE TABLETS

By Florin J. Amrhein

ON page 404, of section 74, in *Methods of Analysis of the Association of Official Agricultural Chemists*, an official method is found for the estimation of strychnine in tablets. This method makes no provision for the addition of interfering fillers, neither for the addition of mineral oil as a lubricant in tablet manufacture. It was found that when mineral oil was used that it produced lowered results in the alkaloidal content using this assay.

The writer set about to discover, if possible, a method of eliminating this source of error. It was found that if mineral oil was used in the manufacture of strychnine tablets that the alkaloid was not completely titratable. Here we have a clear exemplification of Nernst's Law or the theory of the distribution coefficient (Nernst's Law =  $C_2/C_1 = K$ ), where some of the alkaloid remained in the mineral oil used in the manufacture of the tablets. It is true that the quantity of alkaloid that remained untitratable was small, yet it was sufficient to cause appreciable variations in the results. By altering the official method, in order to remove all of the mineral oil, better results were obtained. The alteration in the official method provided for the complete removal of fat or mineral oil. The tablets used in the modified assay were tablets that were taken from commercial lots of strychnine tablets.

### Modified Assay for Strychnine in Tablets

Weigh 25 to 100 tablets and transfer directly to a separatory funnel. Add 20 cc. of water to disintegrate the tablets followed by 1-2 cc. of 10 per cent. sulphuric acid. After complete disintegration has been effected extract twice with two 25 cc. portions of chloroform to remove the fat. Then make alkaline with dilute ammonia water (1 + 2). Extract five times with chloroform, using 25, 20, 15, 10, and 5 cc. portions respectively; or until the alkaloid is completely removed. Combine the first two extractions in a second separatory funnel, into the stem of which has been inserted a pledget of absorbent cotton wet with chloroform. Wash with 5 cc. of water containing a drop of dilute ammonium hydroxide (1 + 2). When clear, filter the chloroform portion into a small beaker. Wash each successive chloroform extract with the same wash water and filter in a

similar manner into the main portion, finally washing the outer surface of the stem of the separatory funnel with a few cc. of chloroform and adding this also to the main portion. Evaporate on a steam bath, removing the beaker from the bath at 3-5 cc. and allow final evaporation to take place in a current of air to prevent decrepitation as the last portions evaporate from the beaker. Add 2-3 cc. of neutral alcohol, cover beaker, and warm on a steam bath to dissolve the residue. Add a few drops of methyl red indicator and titrate with 0.02 N acid to a faint pink color. Add 50 cc. of recently boiled water and continue the titration with 0.02 N acid to a faint red color. One cc. of 0.02 N acid is equivalent to 6.684 mg. of strychnine ( $C_{21}H_{22}O_2N_2$ ), or 8.565 mg. of strychnine sulphate ( $(C_{21}H_{22}O_2N_2)_2H_2SO_4 \cdot 5H_2O$ ), or 7.944 mg. of strychnine nitrate ( $C_{21}H_{22}O_2N_2HNO_3$ ).

TABLE I  
*Results Obtained Using the Modified Method*  
1/40 grain tablet

Sample No.	Collaborator	Amount of Strychnine Recovered
1.	M. J. M.	0.02488 grains
2.	F. J. A.	0.02488 grains
3.	P. S. H.	0.02453 grains
4.	F. J. A.	0.02502 grains
amount of strychnine in 1/40 grain tablet = 0.025 grains		

TABLE II  
1/60 grain tablet

Sample No.	Collaborator	Amount of Strychnine Recovered
5.	M. J. M.	0.01625 grains
6.	R. S. B.	0.01691 grains
7.	S. M.	0.01639 grains
8.	F. J. A.	0.01648 grains
amount of strychnine in 1/60 grain tablet = 0.0166 + grains		

Control analyses were run using the regular A. O. A. C. method and it was found that the results obtained varied from 1/48 to 1/50 of a grain for the 1/40 grain tablet and for the 1/60 grain tablet the assay would indicate that it was a 1/90 grain tablet.

Therefore, it appears to the author that the mineral oil should first be removed as above indicated by the modified assay.

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## TRANSITION POINTS OF MIXTURES OF COW'S BUTTER AND CACAO BUTTER

By David Wilbur Horn and Margaret Alberta Wilson

**T**HE Transition Point of cacao butter is a sensitive characteristic of that substance. Attention has previously been called to this fact by Horn and Osol, working in this laboratory.<sup>2</sup> The Transition Point of cacao butter is certainly affected by the presence of some foreign fats. The discussion in the present paper relates to the effect of added cow's butter upon the Transition Point of cacao butter.

### INTRODUCTION

**RESULTS** We have studied mixtures of cacao butter and cow's butter at intervals of 20 per cent. or less throughout the range of concentrations between 100 per cent. cacao butter and 100 per cent. cow's butter. The Transition Points were well defined until the percentage of cow's butter approached 80 per cent. As far as 70 per cent. there is a linear relation between the Transition Point and the percentage of cow's butter in the mixed fat. This linear relation is expressed by the equation,

$$y = -0.165x + 29.2.$$

In Figure I, our experimental results are represented by heavy black dots, lying along or on the locus of this equation. In Table I, our experimental results are summarized, and are compared with the corresponding figures calculated from this equation.

TABLE I  
SUMMARY OF EXPERIMENTAL RESULTS

Percent of cow's butter, %	Observed Transition Point, in °C.	Calculated Transition Point, in °C.	Difference between observed & calculated
x	y (obs.)	y (calc.)	
0	29.2	29.2	0.0
20	26.2	25.9	+0.3
40	22.6	22.6	0.0
60	19.4	19.3	+0.1
70	17.6	17.6	0.0

<sup>2</sup> The results in this paper are from work submitted by Margaret Alberta Wilson to the Philadelphia College of Pharmacy and Science in partial fulfillment of the requirements for the degree of B. Sc.

<sup>3</sup> This JOURNAL, Vol. 101, p. 611 (1929).



**APPLICABILITY  
TO COMMERCIAL  
CHOCOLATES**

Because this linear relationship persists far beyond the highest concentration of cow's butter ever met with in the mixed fat found in sweet milk chocolates, the Transition Point of the extracted fat may be of use in the factory control of these commercial products. Coatings and chocolates sold as *Milk Chocolates* and as *Sweet Milk Chocolates* are required to contain the fatty and non-fatty milk solids in the proportion normal for whole milk, and must also contain not less than 12 per cent. of total milk solids. In samples of these chocolates examined for the purposes of food control, the quantitative determination of cow's butter rests upon the Reichert-Meissl Number of the extracted mixed fat. We were interested in discovering the Transition Point in the mixed fat to be also a measurable property of the mixed fat, and to be one that can be determined under less exacting conditions than the Reichert-Meissl Number.

**INFLUENCE OF  
VARIABLE  
NATURE OF  
FATS**

Regarding the constant terms in the equation given above, it should not be supposed that we regard the values given here for them as necessarily final, or the constant terms in the equation connecting Transition Points with percentages of cow's butter as single-valued constants in the strict sense. Because of the variable nature of the fatty substances themselves there is reason to expect variations in Transition Points, since the same causes are at work here as produce the well-recognized wide variations in the Reichert-Meissl Number of cow's butter and the lesser variations in the Reichert-Meissl Number of cacao butter. Such unavoidable variations have of course not prevented the Reichert-Meissl Number from acquiring a position of supreme importance, and we see no reason why such variations should have greater weight against the use of the Transition Point.

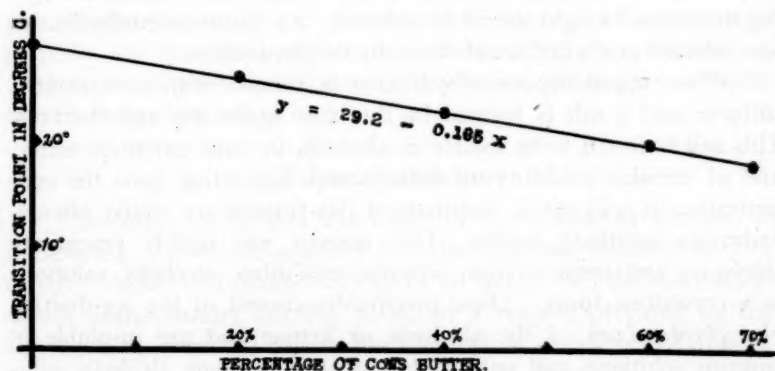
**THE METHOD**

When determining the Transition Points, the melted mixed fat was placed in a Dewar test tube, held firmly in the center of a bath of water and ice. The fat was stirred constantly with a suitable glass stirrer encircling a thermometer arranged with bulb immersed in the fat. After the temperature of the fat had fallen to about 30° C., the readings of the thermometer every minute were written down. The results were then plotted, the temperatures vertically and the times horizontally, yielding in each case a graph suggestive of the root sign  $\sqrt{\quad}$  of algebra. The liquid fat



gradually cooled until at times it had undercooled as much as 5 to 10 degrees, then crystallization set in accompanied by a gradual rise in temperature. This rise stopped at a definite temperature which in our experiments was maintained quite exactly to within one-tenth degree for a period of several minutes. This constant temperature is what we have called the Transition Point.

When discussing the Transition Point as a potentially useful check upon the composition of the mixed fat from sweet milk chocolates, we are not suggesting a substitute for the Reichert-Meissl Number or recommending the Transition Point as equal in all ways to it. We are proposing it as a useful factory check upon successive batches of milk chocolates.



### Heart-Stimulating Action of Camphor Due to Oxidation Product

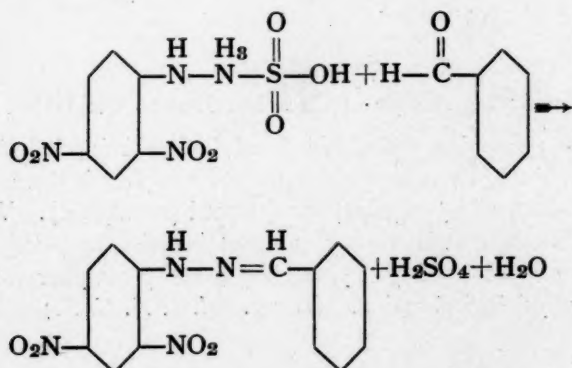
Doctors Asahina and Ishidate of Tokyo Imperial University found that the heart-stimulating action of camphor is due to an oxidation product, allo-*p*-oxycamphor (termed  $\beta$ -camphor). When the camphor is taken, it is usually excreted in urine as *p*-oxycamphor. Chemical oxidation of *p*-oxycamphor gives  $\beta$ -camphor which has a strong physiological action. (*News. Ed. J. A. C. S.*)

# STUDIES IN THE USE OF 2,4-DINITROPHENYLHYDRAZINE AS A QUANTITATIVE REAGENT FOR CARBONYL COMPOUNDS: I. BENZALDEHYDE\*

By R. E. Houghton

ONE of the objections to the use of phenylhydrazine as a quantitative reagent for aldehydes and ketones is the instability of the reagent, due to its tendency to become oxidized. Substituted phenylhydrazones have greater stability and crystallize more readily than unsubstituted phenylhydrazones. The increase in the molecular weight of the substituted phenylhydrazines results in higher melting points for the hydrazones; hence losses due to volatilization on drying to constant weight should be reduced. 2,4-Dinitrophenylhydrazine was selected as a suitable substituted phenylhydrazine.

When 2,4-dinitrophenylhydrazine is treated with concentrated sulfuric acid a salt is formed by the basic hydrazine and the acid. This salt is found to be soluble in alcohols, to some extent in water, and of variable solubility in sulfuric acid, depending upon the concentration of acid used. Solutions of this reagent are, unlike phenylhydrazine solutions, stable. This reagent will readily precipitate aldehydes and ketones from aqueous and dilute alcoholic solutions in a crystalline form. These precipitates consist of the 2,4-dinitrophenylhydrazones of the aldehyde or ketone and are insoluble in aqueous solutions, and only slightly soluble in dilute alcoholic solutions. The equation in the case of benzaldehyde is:



Benzoic acid does not react with 2,4-dinitrophenylhydrazine and herein lies one of the advantages of the method proposed for benzaldehyde.

Brady and Peakin (1) used a 2 N. hydrochloric acid solution of the hydrochloride of 2,4-dinitrophenylhydrazine for quantitative work on three substituted benzaldoximes, filtering on a Gooch crucible, washing with 2 N. hydrochloric acid, and drying at 100 degrees C. to constant weight.

Fernandez and Socias (2) used a 1 per cent. solution of 2,4-dinitrophenylhydrazine in 10 per cent. sulfuric acid for the precipitation of santonin from an alcoholic solution, filtered on a filter plate, washed with 45 per cent. alcohol, and dried to constant weight.

Torres and Brosa (3) used a solution of 0.36 gram of 2,4-dinitrophenylhydrazine in 25 cc. of water and 2.5 cc. of concentrated sulfuric acid for the determination of hexetone (6-m-menthene-5-one) from an alcoholic solution. They claim quantitative precipitation in forty-eight hours.

### Experimental Part

The following method was found to be the most satisfactory of those tried. One-tenth gram of benzaldehyde was dissolved in 5 cc. of ethyl alcohol and diluted with 50 cc. of water. To this were added slowly with constant stirring 50 cc. of a reagent prepared by dissolving 0.25 gram 2,4-dinitrophenylhydrazine in 2.5 cc. of concentrated sulfuric acid with the aid of heat and diluting to 50 cc. with water. The precipitate was stirred until upon standing it settled to the bottom instead of rising to the top. The precipitate was allowed to digest over night and was filtered off on a tared Gooch crucible, washed with about 15 cc. of 2 N. sulfuric acid and then with water until a portion of the washings gave no precipitate with barium chloride, then dried in an oven at 110 degrees C. to constant weight.

The precipitates may be dried in an oven at 110 degrees C. to constant weight in about an hour and a half, but darken and increase in weight slightly upon further heating. Digestion of the precipitates over night and thorough stirring are necessary to reduce occlusion of the reagent and to facilitate filtration. The following table gives the results of duplicate determination on ten samples of benzaldehyde.

Results of Duplicate Determinations		Difference
94.89%	94.43%	.46%
87.50%	87.92%	.42%
96.98%	97.64%	.66%
94.20%	94.51%	.31%
95.46%	95.65%	.19%
94.28%	94.29%	.01%
93.46%	93.72%	.26%
92.89%	92.92%	.03%
94.91%	94.31%	.60%
90.55%	90.96%	.41%

### Summary

A new method for the quantitative determination of the degree of purity of benzaldehyde by the use of 2,4-dinitrophenylhydrazine has been proposed. It is thought that this method is more accurate than the other methods in common use. The method is rapid, simple and economical. The study of the use of 2,4-dinitrophenylhydrazine as a reagent for carbonyl compounds is being continued.

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\*Abstracted from the dissertation of Richard Everett Houghton presented May 10, 1933, to the Faculty of the Philadelphia College of Pharmacy and Science in partial fulfillment of the requirements for the degree of Bachelor of Science in Chemistry.

## SOLID EXTRACTS

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*Smoker's cancer has been blamed upon tobacco tar. And many an old pipe, long subjected to the destructive distillation of the "filthy weed," carries in its stem an unhealthy share of noxious tar—to say nothing of what might be in the worm condenser at the receiving end. However, investigators have recently found that tobacco tar, which has been alleged by some advertisers of special smoking equipment to be a potential source of mouth cancer, was wholly inactive in producing cancers under conditions in which gas-house tars of recognized carcinogenic action produced cancers invariably. This investigation indicates strongly that whatever may be the cause of smoker's cancer, the tar present in tobacco smoke is not responsible.*

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Urea is now a useful industrial and agricultural chemical. Famous as the first example of the "synthesis" of organic chemicals—and long known as a constituent of kidney effluent, it now finds multifarious uses. Yet Philadelphia throws away twelve thousand pounds of it into the Delaware Bay each day—with its compliments to Chester and Wilmington.

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*The "Electrynx" is the new electric tongue. It is a compact, inexpensive little instrument which promises a real usefulness, indicating the acidity or concentration of weak solutions such as saliva, fruit juices or blood. It may be useful in such varied applications as grading fruits or vegetables, testing the hardness or salinity of water, the acidity of beverages and petroleum products or controlling food and dairy products.*

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To what does an ordinary cake of chocolate owe its nutritional and stimulant value? Most persons will answer: to sugar.

Yet chocolate variably contains from 30 to 40 per cent. of cacao butter, a very nutritional fat—to say nothing of the physiological kick in the caffeine like alkaloid which it also contains.

*How much nicotine is there in the ordinary cigar?—leaves one wondering as to what constitutes an ordinary cigar. Curiosity prompted the weighing of four standard three-for-a-quarter brands in the nude. The average dry weight was just short of ten grams (a third of an ounce)—which makes the average cigar tobacco—equal to about ten ordinary cigarettes.*

*The nicotine content of the unsmoked cheroot also varies, around 1½ per cent., which means that it contains a little over 2 grains of nicotine alkaloid—a poisonous dose.*

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It is not to be presumed, however, that all the nicotine in the unsmoked cigar invades the constitution of the smoker, whether he inhales or not. Most of it is burned in the combustion—and the drier the cigar the greater the nicotine loss, moisture in the tobacco conserving its toxic constituent. Much nicotine condenses in the “butt,” which perhaps explains the extra potency charged against the salivated “stump.”

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*Lord Rutherford, the famous English physicist, has suggested the name diplogen for heavy hydrogen and the name diplon for the nucleus of the atom of heavy hydrogen. Hitherto the name deuterium has been used for the former, and deuton, or deuteron, for the latter. Lord Rutherford acknowledged that the name given by a discoverer was generally adopted by the scientific world, but he regarded the question as of great scientific importance in the case of heavy hydrogen, and thought that deutons were liable to be confused with neutrons (especially if one had a cold!!) As neutrons were involved in any discussion of heavy hydrogen, the question of confusion is very pertinent.*

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The average American drinks the essence of twelve pounds of roasted coffee each year, yet few people know how to make or drink this famous beverage.

One-half the soluble constituents of roasted coffee is a tannin substance—of the same nature as the compounds that make leather from animal hide—and roasted coffee also contains nearly 15 per cent. of oil (or fat).



## SCIENTIFIC AND TECHNICAL ABSTRACTS

Compiled by Arthur Osol, Ph. D.

*The Decomposition of Acetylsalicylic Acid in Aqueous Solutions.* C. Morton. *Quart. Journ. Pharm. Pharmacol.* 6, 492-5 (1933). The velocity of decomposition of acetylsalicylic acid in aqueous solutions in the presence of alkali-metal citrates and acetates has been determined, and a composite graph is given from which the percentage hydrolysis at any period during storage can be read. The rate of decomposition is independent of the absolute and relative concentrations of the acetylsalicylic acid and alkali-metal salt, but increases very rapidly with rise of temperature. At room temperatures, all of the solutions investigated decomposed to the extent of over 10 per cent. during the first day, or approximately 50 per cent. in the course of a week.

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*A New Method for the Determination of Elemental Sulphur.* Noel L. Allport, *Quart. Journ. Pharm. Pharmacol.* 6, 431-35 (1933). A rapid method is proposed which depends upon the conversion of sulphur to thiocyanate by the use of an aqueous solution of potassium cyanide and triethanolamine. The method is applicable to precipitated and sublimed sulphur, as well as ointment of sulphur, compound licorice powder, confection of sulphur and sulphur lozenges. The material to be assayed, containing about 0.1 gram of sulphur, is accurately weighed into a conical flask of about 175 cc. capacity. Fifty cc. of reagent (potassium cyanide 40, triethanolamine 90, water to make 1000) is added together with 1 gram of simple ointment or soft paraffin. (The latter addition is not necessary in the case of ointments made with paraffin base.) After adding a little granular pumice to prevent local superheating, the flask is connected to a reflux condenser and the contents vigorously boiled for 30 minutes. After cooling, 10 cc. of formaldehyde solution is added, the mixture acidified with dilute nitric acid, and exactly 50 cc. of N/10 silver nitrate added. If the material being assayed has colored the liquid, as occurs with compound licorice powder, it is necessary to add about 0.5 gram of decolorizing charcoal. In any case, the mixture is filtered through an asbestos pad by means of a Buchner filtering funnel and the residue washed with water. The filtrate is

titrated with N/10 ammonium thiocyanate solution, ferric alum being used as the indicator. To determine the value of the blank on the reagent, 50 cc. is mixed with 10 cc. of formaldehyde solution, the mixture acidified and titrated as already described. One cc. of N/10 silver nitrate is equivalent to 0.003206 gram of sulphur.

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*Linimentum Ammoniatum.* (D. A. B.) Wolfgang Brandrup. *Pharm. Zentralhalle*, 74, 749-51, (1933). *Linimentum ammoniatum* is considered to be an emulsion in which aqueous ammonia is the dispersion medium, the oil is the dispersed phase and the small quantity of ammonium soap formed, together with the added soap, is the emulsifier. The author finds that a better emulsion may be made if oleic acid is added to the oil mixture. The addition of 0.5 per cent. oleic acid (producing an acid value of 4.6) yielded an emulsion with large irregular oil globules, while with 2 per cent. oleic acid (acid value 20.4) an emulsion containing small regular oil globules was obtained. With greater acidity the emulsions were too viscous. It is recommended that the formula of the D. A. B. be modified by the addition of sufficient oleic acid to obtain an acid value of 6, corresponding to the addition of approximately 0.7 per cent. oleic acid. The resulting product can be poured readily.

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*Microanalysis of Magnesium with o-Oxyquinoline.* Georges Glomaud. *Journ. Pharm. et Chim.* 19, 14-29 (1934). Magnesium is determined by adding an excess of 2 per cent. solution of oxyquinoline in 95 per cent. alcohol and 1 cc. of ammonia water to a 10 cc. portion of the sample to be tested. After heating on a water bath for 5 minutes, the precipitated magnesium o-oxyquinolate is filtered through a Jena (12 G 4) micro-filter, washed with three 5 cc. portions of 2 per cent. solution of ammonia and finally decomposed by treatment with 10 to 15 cc. of dilute hydrochloric acid (1-10). The liberated o-oxyquinoline is determined by adding 5 to 10 cc. of a solution of potassium bromide (40 grams in 100 cc.) and an excess of tenth-normal bromine solution after which the mixture is shaken carefully for 30 seconds and the excess bromine determined by adding potassium iodide and titrating with tenth-normal sodium

thiosulphate solution. Each cc. of the bromine solution consumed corresponds to 3.63 milligrams of oxyquinoline or 0.304 milligram of magnesium. For very small quantities of magnesium a weaker bromine solution may be used. The method has been found to be satisfactory for the determination of 0.1 milligram of magnesium. A gravimetric method is also described in which the precipitated magnesium derivative is weighed after drying to constant weight at 105 degrees C.

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*Nitron as a Precipitant for Nitrates.* J. E. Heck, H. Hunt and M. H. Mellon. *The Analyst*, 59, 18-25, (1934). In view of the voluminous character and complex structure of some of the precipitates formed by certain elements with various organic precipitating agents, the authors have undertaken an investigation to determine whether such precipitates entrain certain cations, and if so, whether the magnitude of contamination is sufficient to influence seriously the precision of analytical determinations. The investigation also included a study of the reproducibility of individual determinations and the reliability of the methods under different conditions. From the organic reagents available, nitron, a precipitant for the nitrate radical, was chosen for the first work. This compound seemed particularly promising, on account of the possibility of oxidizing and volatilizing the precipitate of nitron nitrate, leaving as a residue only material which had been entrained or incompletely removed during washing. This residue could then be examined spectroscopically or taken up in a solvent and tested colorimetrically.

In the precipitation, a solution containing about 0.12 gram of nitrate in 100 cc. was acidified with 12 to 15 drops of dilute sulphuric acid (2-3) and heated almost to boiling. To this was added, in one portion, 12 cc. of a 10 per cent. solution of nitron in 5 per cent. acetic acid. After cooling to room temperature, the beaker was placed in ice water for 1½ hours. The precipitate was quickly transferred to a porous bottom crucible, washed with not more than 12 cc. of ice-cold water and dried to constant weight at 105 degrees C. The nitrate content was calculated by means of the theoretical factor 0.1653.

The following conclusions were reached. (1) Entrainment, either of metallic cations or of precipitant, did not occur to an extent

sufficient to influence appreciably the precision of analytical results. (2) The reproducibility of individual determinations was satisfactory, considering the solubility of the precipitate. (3) The reliability of the method varies for the different systems studied, if one assumes that the nitrate present is equivalent to the amount of metal found by a direct determination.

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*The Determination of Alcohol in Anesthetic Chloroform.* R. Fabre and D. Brard. *Journ. Pharm. et Chim.* 19, 5-14, (1934). The alcohol in 5 cc. of chloroform is extracted by agitation with three 10 cc. portions of distilled water which are subsequently combined and diluted to 100 cc. A 5 cc. portion of this solution is introduced into a glass-stoppered tube containing 4.1 cc. of 66 per cent. sulphuric acid and 5 cc. of a solution of 2 grams of potassium dichromate in 1000 cc. After heating on a water bath at 85 degrees C. for one hour to effect oxidation of the alcohol, the tube is cooled and the excess of dichromate reduced with 5 cc. of a solution of ferrous ammonium sulphate (7.6 grams per liter). The excess Mohr's salt is determined by titration with N/100 potassium permanganate. A blank titration is carried out with 5 cc. of the Mohr's salt solution. If N represents the cc.'s of permanganate required in the blank and N' the cc.'s required in the determination, the alcohol content (in grams per 1000 grams of chloroform) is calculated as follows:

$$[10 - 0.4906 (N - N')] \times 20$$

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$$4.262 \times 7.475$$

In this formula 0.4906 milligram represents the dichromate equivalent to 1 cc. of N/100 potassium permanganate; 4.262 is the quantity of dichromate equivalent to 1 milligram of alcohol and 7.475 grams is the weight of 5 cc. of chloroform. The method is reported to be much shorter and considerably more accurate than that given in the French Pharmacopœia.

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*A Volumetric Method for the Determination of Barium and of Sulphates.* J. C. Giblin, *The Analyst*, 58, 752-53 (1933). The use of the sodium salt of rhodizonic acid was suggested by Feigl for the

detection of barium and strontium. When spotted on filter paper, this reagent gives a reddish-brown color with barium or strontium in neutral solution. On acidification, the barium spot becomes bright red or pink, whereas the strontium color is destroyed. The author has adapted this method to the volumetric determination of sulphates and of barium in acid solutions. Preliminary work showed that the reagent did not work well when used as an internal indicator, or even when drops were placed in depressions on a white tile. The following method was found suitable. Drops of the indicator were spotted on filter paper. In the determination of sulphuric acid, barium chloride solution was added from a burette and the contents of the flask were well mixed. The precipitate was allowed to settle, and drops of the supernatant liquid were removed and spotted on the filter paper. The appearance of a pink or red color indicated the completion of the reaction. The reverse titration was carried out in the same manner until drops taken from the supernatant liquid ceased to give a red color on filter paper. Results of reasonable accuracy were obtained.

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*A Rapid Colorimetric Method for the Detection and Determination of Small Quantities of Oxygen in Gases.* H. R. Ambler. *The Analyst*. 59, 14-15, (1934). A colorimetric method has been worked out for the detection of oxygen in mixed gases, and for its determination where present in quantities between 0.01 and 0.5 per cent. The volume of sample required is 20 cc. or less, depending on the oxygen content. The principle of the process depends on the color imparted to alkaline pyrogallol solution, which is compared with that of iodine solutions of known strength. A table, showing the relationship between concentration of oxygen and normality of standard iodine solution is given for use in approximate work. The method was applied originally to coal gas; hydrogen, hydrocarbons and oxides of carbon not interfering. Nitrous oxide also, has been found not to interfere. Hydrogen sulphide (which gives a red color) and oxidizing gases, such as chlorine, must not be present.



## ABSTRACTED AND REPRINTED ARTICLE

### HEAVY HYDROGEN: A SIGNIFICANT DISCOVERY\*

By Ernest Bowman Ludlam, M. A., D. Sc.

Abstract of an Address Given to an Evening Meeting in Edinburgh on  
December 15th

**I**T is not too much to say that the recent discovery of a new kind of hydrogen has created something of a sensation in the scientific world. Since the discovery of hydrogen 150 years ago it has been subjected to continual examination, and its atomic weight relative to oxygen has been determined with the most meticulous care, but it was only two years ago that any suspicion arose that it might possibly contain two different kinds of atom.

In 1929 a study of the absorption band spectrum of oxygen in the atmosphere showed that oxygen contained an isotope of mass 18. Later, this was proved to be present in the proportion of about 1 in 650. The chemical atomic weight,  $O = 16$ , is an average value, and the common oxygen atom must have a weight a little less than 16. This threw out the accepted value of the ratio of the hydrogen atom to the oxygen atom, but if hydrogen also had an isotope of mass 2, in the right amount, it would bring things right again. In May, 1931, Birge suggested that an isotope of hydrogen might exist with atomic weight 2 and in the proportion of about 1 part in 4500 of ordinary hydrogen.

The discovery of a second kind of hydrogen is of the greatest significance, and its name is being discussed internationally. The Americans have proposed the name "deuterium," but in a discussion at the Royal Society in London on December 14 Lord Rutherford suggested the name "diplogen." Urey, in New York, examined the atomic spectrum of hydrogen very carefully and found a very fine line at exactly the right distance from the red hydrogen line. He concentrated the heavy hydrogen by evaporation of liquid hydrogen

\*Reprinted from the *Pharmaceutical Journal*, London, England.

and found that he had then increased the intensity of the new line. Then experimenters in several countries set to work to concentrate the heavy hydrogen. The most successful of these was G. N. Lewis, of California, who found that continued electrolysis of an aqueous solution of sodium hydroxide concentrated the heavy water in the residue. In March of 1933 Lewis had obtained water of density 1.03, i. e., about 30 per cent. of the hydrogen in it was of atomic weight 2.

Heavy water had now been obtained quite pure, and had the following properties:

Density .....	1.105
Freezing point .....	3.8° C
Boiling point .....	101.42° C
Temperature of maximum density.....	11.6° C

Electric conductivity two-thirds of ordinary water

Nearly ten years ago, under Professor Kendall's direction, some interesting research work was done proving that the isotopes of mercury could be separated, to some extent, by electrolysis. This suggested a research on the prediction made by Birge as to isotopes of hydrogen, and a good deal of work in that connection had been done in the Edinburgh University. This work corroborated and, as a matter of fact, very nearly anticipated, the results obtained by the American investigators.

If water contained only this heavy form of hydrogen our ponds would freeze at 39 degrees F. instead of 32 degrees F., our kettles would boil at 214.5 degrees F. instead of 212 degrees F., and its maximum density would be at 52 degrees F. By the chemist the behavior of this new hydrogen will be watched with interest, as it takes part in those reactions and in aqueous solutions where ordinary hydrogen has evaded observation. The organic chemist, may, however, be able to produce five different methanes, and thirty-two ethyl alcohols, of which eight pairs will be optical isomers. It is too early to predict what may be possible in the realms of botany and biology, but as indications it may be mentioned that tobacco seeds which sprouted in two days and gave good seedlings in two weeks in

ordinary water, did not germinate in heavy water; in 50 per cent. heavy water and ordinary water the development proceeded at half the normal rate. Comparative experiments with water (a) containing 92 per cent. of heavy water, and water (b) containing 30 per cent. of heavy water were tried on the following organisms:

- (1) Tadpoles (a) dead in one hour; (b) unaffected after twenty-four hours.
- (2) Aquarium Fish (a) dead in two hours; (b) no effect in twenty-four hours.
- (3) Flatworms (a) dead in three hours; (b) uninjured in three days.
- (4) Paramecium (a) dead in twenty-four hours; (b) no effect in three days.

Apparently heavy hydrogen slows down the life processes, and the higher the form of life the more pronounced is the effect. When pure, it might inhibit life altogether. Chemists may have to keep it in bottles labelled "Poison." When we reflect on the extraordinary specific power of the biological organism, its uncanny power of selecting or rejecting, the marvellous sensitiveness of the balance of living matter and the growth and development of man himself, we await with eagerness—perhaps even trepidation—the results to pharmacology of the addition to the British Pharmacopœia of the new and potent drug, heavy water! Already, there has been one remarkable scientific application of heavy hydrogen. When used as a minute projectile, flung against other atoms with enormous speed, it batters and disrupts them. It thus becomes a powerful weapon in the modern line of research for transmutation of the elements.

In the discussion at the Royal Society on December 14, Professor Soddy is reported as saying that he wanted to protest as forcibly as he could against the description of heavy hydrogen as an isotope. He had not seen any evidence that we were not dealing with something like the difference between oxygen and ozone. The answer to Professor Soddy is quite clear in the literature relating to heavy hydrogen. There have been shown on the screen tonight the heavy hydrogen lines in the spectrum. These lines are produced by the atom, and they are atomic lines. A molecule, like ozone, gives a band

spectrum. It is clear that we are dealing with an isotope. Hydrogen is so fundamentally important that it is impossible to place limits to the far-reaching results of this new discovery.

### Avocado Oil, Its Physical and Chemical Characteristics

	25°	
Specific Gravity	25°	0.921
Refractive Index	20°	1.470
Acid Value		2.5
Saponification Value		192.6
Unsaponifiable matter (per cent.)		1.4
Iodine Number (Hanus)		94.4
Acetyl Value		9.2
Reichert-Meissl Number		1.6
Polenske		0.2
Saturated Acids (corrected) (per cent.)		7.6
Unsaturated Acids (corrected) (per cent.)		85.0
Iodine Number of Unsaturated Acids		101.2
Chemical Composition—		
Glycerides of:		
Oleic Acid		77.3
Linolic Acid		10.8
Myristic Acid		trace
Palmitic Acid		6.9
Stearic Acid		0.8
Arachidic Acid		trace
Unsaponifiable Matter		1.5

The keeping qualities of the oil are excellent, Jamieson reported samples kept in partially filled bottles in the laboratory for a year, with but a slight increase in free fatty acid.—*Drug and Cosmetic Industry*, Dec. 1933, p. 534.

## BOOK REVIEWS

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**BACTERIOLOGY AND SANITARY SCIENCE.** By Louis Gershenfeld, B. Sc., P. D. Professor of Bacteriology and Hygiene and Director of the Bacteriological and Clinical Chemistry Laboratories in the Philadelphia College of Pharmacy and Science. 2d Edition. Published 1933. Octavo, 439 pages, illustrated with 55 engravings and 3 plates. Cloth, \$4.50, net.

This book is the outgrowth of lectures delivered to students in pharmacy, chemistry and bacteriology in the Philadelphia College of Pharmacy and Science during the past fifteen years. The second edition has been thoroughly revised and enlarged to include every advance in the various fields, and many changes and additions have been made in every section.

The layman most frequently turns to the pharmacist, the chemist, the bacteriologist, or the nurse, rather than to the physician, for information on sterilization, disinfection, fumigation, insecticides, deodorants and other questions on sanitation, and it is to these public health workers that this book will be most helpful.

Obviously, in a book of this size, no attempt could be made to give detailed descriptions of the many characteristics of bacteria and animal parasites. The author, however, has presented an outline of these, which is sufficient for the reader to understand the principles involved, and to grasp the fundamental applications. For the same reason it is also apparent that many modifications of techniques could not be included. Only those methods, which have withstood the acid test of practical application have been included.

The book is divided into four parts. Part I discusses the general characteristics, activities and classification of bacteria in concise, but complete form. Then in similar form, follows discussions on the following: Apparatus and Methods of Studying Bacteria, Stains and Staining; Culture Media; Sterilization; Disinfection; Fumigation; Fungi, Bacteria Useful in Commerce and Industry; Pathogenic and Non-Pathogenic Bacteria.

Part II is devoted to animal Parasitology. Much valuable information is given on insecticides and insect extermination.

In Part III will be found a study of Infection, Immunity, Allergy and Biological Products. The pharmacist and those engaged



in the profession of medical care should find in this section much valuable information. Chapter XXII should prove to be especially interesting to public health workers. It is devoted to Biological Products and under this caption will be found many pertinent facts concerning: Federal Control; Labeling and Dating; Storage, Preparation of Diphtheria and Tetanus Antitoxin and their Uses; Scarlet Fever Streptococcus Toxin; and North American Anti-Snake Bite Serum.

The exclusive feature of Part IV is Sanitary Science. The author discusses such factors as: Atmospheric Conditions, Ventilation and Heating, Disposal of Waste, Sewage, etc., Water and Water Purification, Milk and other Foods.

The appendix contains information on Diseases of Unknown, Doubtful or Not Definitely Determined Etiology.

The book is well indexed and remarkably free from typographical errors. It should prove to be a valuable addition to the library of all those connected either directly or indirectly with public health work.

R. L. C.

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BENTLEY AND DRIVER'S TEXTBOOK OF PHARMACEUTICAL CHEMISTRY. 2d Edition. Revised by John Edmund Driver, Ph. D., M. Sc., A. I. C. London: Oxford University Press, 1933. 538 pages, illustrated with 40 engravings and 1 plate. Cloth, 16s.

The first edition of this textbook was published in 1925, the second impression revised in 1929 and now we have this second edition revised by Dr. Driver, who is a lecturer on chemistry in the University College of Nottingham. This volume follows closely the publication of the 1932 edition of the British Pharmacopœia and the author acknowledges this as the source of much material.

The text is arranged in three parts with an appendix. Part I is concerned with a general consideration of the methods by which the purity of pharmaceutical substances is determined. Such subjects as the use of physical instruments, the preparation and use of volumetric solutions, and the determination of pH values are collected together.

Chapter VI is devoted to an outline of the official limit tests for chlorides, sulphates, iron, arsenic and lead. The author states that

while the Gutzeit method of testing for arsenic is rapid, convenient and delicate, yet it is inferior, both in accuracy and as regards the certainty of the results, to the famous Marsh-Berzelius Test in which permanent mirrors of arsenic are produced. He also states that the Gutzeit stains are sensitive to light, and are greatly affected by damp and foreign gases. He might well have added that while the mercuric chloride paper may in some instances show no coloration in daylight they may exhibit distinct evidence of staining when viewed in ultra-violet light.

Part II deals principally with the inorganic compounds in frequent use in pharmacy, although the organic salts of metals are, for convenience, included in this section. A brief general discussion of the chemistry of each element is followed by a description of such derivatives as are defined in the monographs of the British Pharmacopœia.

Part III presents a systematic account of organic chemistry, beginning with a discussion on the elements present in organic compounds and then in sequence follows such subjects as: Hydrocarbons of the Paraffin Series, Unsaturated Hydrocarbons, Alcohols, Ethers, Aldehydes and Ketones and so on, concluding with alkaloids and alkaloidal assays and other substances of pharmaceutical importance or interest.

The appendix includes among other topics: Tables for the identification of inorganic substances, notes on the identification of organic compounds, and acid and alkali indicators.

The text is notably free from errors and many references are mentioned for those who might desire to make a more detailed study of some particular subject. The index is complete, the illustrations clear, and the style interesting and enjoyable.

R. L. C.